

**AMENDMENTS TO THE DRAWINGS**

The attached sheets of drawings are replacement sheets for Figures 9A-9D and 10A-10G (originally Figures 9 and 10).

Attachment:      Annotated sheets showing changes  
                         Replacement sheets

**REMARKS**

This is a full and timely response to the Office Action mailed August 26, 2004, submitting concurrently with a one month Extension of Time to extend the due date for response to December 26, 2004.

By this Amendment, claims 1, 3, 5 and 7-10 have been amended to place the claims in better form under U.S. practice and to more particularly define the present invention. Further, claim 12 has been added to further protect specific embodiments of the present invention. Lastly, claims 2 and 6 have been canceled without prejudice or disclaimer to their underlying subject matter. Support for the claim amendments and new claim can be found throughout the specification and the original claims, see, Examples 1 and 5-7 of the specification and in particular, page 16, lines 13-15, page 24, line 1-3, and page 22, lines 20-22. Claims 1, 3, 5 and 7-12 are pending in this application.

In view of these amendments, Applicant believes that all pending claims are in condition for allowance. Reexamination and reconsideration in light of the above amendments and the following remarks is respectfully requested.

**Objection to the Drawings**

Applicant has amended the labels of Figures 9 and 10 to Figures 9A-9D and 10A-10G as per the Examiner's request. Thus, withdrawal of this objection is respectfully requested.

**Objection to the Specification**

Applicant has amended the specification to identify in the Brief Description of the Drawings the SEQ ID NOS. of Figures 9 and 10. Applicant has also amended the specification to identify the SEQ ID NOS. for the sequences on pages 25-27 of the specification. Thus, withdrawal of this objection is respectfully requested.

**Objection to the Claims**

Applicant has amended the claims to address each issue raised by the Examiner. Specifically, claims 1-6 have been amended in accordance with the Examiner's suggestions or canceled. Further, claims 8 and 9 have been amended to introduce the proper article. However, Applicant notes that such an amendment should not limit the "cell" and "seed" to a singular form

since, under U.S. practice, the article “A” means one or more. Lastly, claim 7 has been amended as per the Examiner’s request.

### **Rejections under 35 U.S.C. §112**

Claims 1-11 are rejected under 35 U.S.C. §112, second paragraph, for alleged indefiniteness. Applicant respectfully traverses this rejection.

However, in order to expedite prosecution, Applicant has amended claims 1 and 3 to clarify the claimed invention and address the Examiner’s concerns. Also, claim 6 has been canceled thereby alleviating the Examiner’s concerns. Further, claim 1 has been amended to now direct to a method for producing a transgenic gramineae by transforming a gramineae with the claimed polynucleotide. Also, claim 3 has been amended to clarify that the polynucleotide further comprises the promoter CaMV35S.

Thus, in view of these claim amendments, withdrawal of this rejection is respectfully requested.

Claims 1-11 are rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to enable the claims. Applicant respectfully traverses this rejection.

However, in order to expedite the allowance of the present application, Applicant has amended the claims to direct to a “*polynucleotide is selected from the group consisting of (A) a polynucleotide encoding an amino acid sequence of SEQ ID NO: 1, (B) a polynucleotide encoding an amino acid sequence of SEQ ID NO: 2, (C) a polynucleotide which encodes an enzyme exhibiting nicotianamine amino transferase (NAAT) activity and can hybridize with polynucleotide (A) or (B) under stringent conditions of a hybridization buffer comprising 6 x SSPE, 5 x Denhart solution, 0.1% SDS, and 100 mg/ml altered salmon spermary DNA, and a hybridization temperature of 65 degrees, and (D) a polynucleotide comprising the base sequence of SEQ ID NO. 3*” which Applicant believes satisfy the enablement requirement under U.S. practice.

The Examiner has indicated that the “stringency condition’ in the claims, specifically claim 6, includes any low, moderate and high stringency conditions. Applicant has addressed the Examiner’s concerns by defining specific hybridization conditions of high stringency *of a hybridization buffer comprising 6 x SSPE, 5 x Denhart solution, 0.1% SDS, and 100 mg/ml altered salmon spermary DNA, and a hybridization temperature of 65 degrees.*

Two experiments in the specification, a transformation with NAAT cDNA (Examples 1 to 4) and a transformation with NAAT genomic DNA (Examples 7 and 8), provide the evidence that a polynucleotide encoding an enzyme exhibiting NAAT activity is capable of inducing iron-deficiency resistance in graminaceous plants. Also, anyone skilled in the art can isolate a polynucleotide that encodes an enzyme exhibiting NAAT activity under stringent conditions in which the hybridization buffer comprises 6 x SSPE, 5 x Denhart solution, 0.1% SDS, and 100 mg/ml altered salmon sperm DNA, and the hybridization temperature is 65 degrees (See Example 5). Therefore, given the teachings in the specification, one skilled in the art can produce the claimed transgenic gramineae having iron deficiency resistance without undue experimentation.

Thus, withdrawal of this rejection is respectfully requested.

Claims 1-11 are rejected under 35 U.S.C. §112, first paragraph, for allegedly lacking written description of the claimed invention. Applicant respectfully traverses this rejection.

However, in order to expedite the allowance of the present application, Applicant has amended the claims to direct to a “*polynucleotide is selected from the group consisting of (A) a polynucleotide encoding an amino acid sequence of SEQ ID NO: 1, (B) a polynucleotide encoding an amino acid sequence of SEQ ID NO: 2, (C) a polynucleotide which encodes an enzyme exhibiting nicotianamine amino transferase (NAAT) activity and can hybridize with polynucleotide (A) or (B) under stringent conditions of a hybridization buffer comprising 6 x SSPE, 5 x Denhart solution, 0.1% SDS, and 100 mg/ml altered salmon sperm DNA, and a hybridization temperature of 65 degrees, and (D) a polynucleotide comprising the base sequence of SEQ ID NO. 3*” which Applicant believes satisfy the written description requirement under U.S. practice.

Thus, withdrawal of this rejection is respectfully requested.

### **Rejection under 35 U.S.C. §101**

Claims 8 and 9 are rejected under 35 U.S.C. §101, for allegedly being directed to non-statutory subject matter. Applicant respectfully traverses this rejection.

However, in order to expedite prosecution, Applicant has amended claims 8 and 9 to a seed or cell comprising the claimed polynucleotide which addresses the Examiner's concerns.

Thus, withdrawal of this rejection is respectfully requested.

**Rejection under 35 U.S.C. §102**

Claims 1-9 and 11 are rejected under 35 U.S.C. §102(a) as allegedly being anticipated by Satoshi et al. (EP 0860499, hereinafter EP '499). Applicant respectfully traverses this rejection.

To constitute anticipation of the claimed invention under U.S. practice, the prior art reference must literally or inherently teach each and every limitation of the claims. Here, in this case, Satoshi et al. do not teach the claimed limitation “*transforming a gramineae with a polynucleotide by using a vector pIG121Hm or pBGRZ*”.

Thus, withdrawal of this rejection is respectfully requested.

**Rejection under 35 U.S.C. §103**

Claims 1-11 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Mori Satoshi (*S. Mori*, “*Reevaluation of the genes induced by iron deficiency in barley roots*”, *Soil Sci, Plant Nutr.*, 43, pp. 975-980 (1997)). Applicant respectfully traverses this rejection.

To establish a *prima facie* case of obviousness, the prior art reference must either alone or in combination teach or suggest the invention as a whole, including all the limitations of the claims. Here, like EP '499, Mori Satoshi does not teach the claimed limitation “*transforming a gramineae with a polynucleotide by using a vector pIG121Hm or pBGRZ*”.

Mori Satoshi notes the desire of making “transgenic cultivars tolerant to Fe-deficiency by introducing Fe-regulated genes in the biosynthesis of mugineic acids into plants susceptible to Fe-deficiency” (see page 975, left column, line 11-15, of the reference). However, there is no teaching or suggestion in the reference about how to introduce a gene of an enzyme in the biosynthesis pathway of mugineic acids (especially, a NAAT gene) into plants susceptible to Fe-deficiency (especially, a graminaceous plant).

In order to express a gene in a graminaceous plant, a promoter, vector and terminator suitable for graminaceous plant must be selected, and integrated into a precise construct to express the gene in the graminaceous plant. It was difficult prior to the present application filing date to introduce a gene (especially, a long construct of a gene) into graminaceous plants. In the reference, it is not specified which promoter should be combined with which vector to make a

transformation construct, and how a graminaceous plant should be transformed with the obtained construct.

Further, even though the NAAT gene is expressed in graminaceous plant, it cannot be predicted whether the plant would have iron-deficiency resistance because the expression of the enzyme in the mugineic acid biosynthetic pathway may be harmful to plants. For example, it is well known that excess iron in a plant causes damage to the cell due to the highly reactive radicals produced by the fenton reaction.

On the other hand, the present inventors finally succeed in transformation by using a *pIG121Hm* or *pBGRZ* vector, CaMV35S promoter or native NAAT promoter, TNOS terminator or native NAAT terminator and agro-bacterium mediated transformation technique. The present invention demonstrates for the very first time that an iron-deficiency resistant gramineae can be obtained when a polynucleotide encoding an enzyme exhibiting NAAT activity is introduced into a gramineous plant. Further, the present invention also unexpectedly demonstrates that the transgenic plants of the present application are able to vigorously grow even in a calcareous alkaline soil.


Thus, for these reasons, withdrawal of this rejection is respectfully requested.

### CONCLUSION

For the foregoing reasons, all of the claims now pending in the present application are believed to be clearly patentable over the outstanding rejections. Accordingly, favorable reconsideration of the claims in light of the above remarks is courteously solicited. If the Examiner has any comments or suggestions that could place this application in even better form, the Examiner is requested to telephone the undersigned attorney at the below-listed number.

Dated: December 27, 2004

Respectfully submitted,

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Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 180013 for any such fees; and applicant(s) hereby petition for any needed extension of time.

Application No.: 10/019,783

Docket No.: SAE-0005

**ANNOTATED SHEETS**





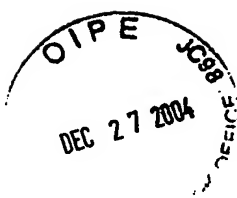


FIG. 9B

ATGCATCCAACATAATTACTTCAAATTCAAATTCAAATTACATTCTTCCGTACATATTTT  
TGAAGATGCATGTATTTTAAGAATAATGACGAGAGCTAAAGTTATGCTACGACTAATCAT  
CTGGATATCCTTTGTCCATCTTTTGTATATACTGTGGAATGTTAATGGTCAAATCATATT  
ACACAAATATCCATGCTAGTTTCTAGAAAGATTGATTATTTTCTGTAAACCATGAACTCC  
GTATTAACTTCCATGTAAACAGGTGAACTGAACTTACATCTTTTGGAGGAAAATAGACGA  
TGACATTGATTTTTTGCTGCAAGCTCGCAAAAGAAGAATCAGTAATCTTATGCCAGGTAG  
GAATCCATTGTTGATTTTTGACTGTATATGAAGTTCTTATCAATTTCCGAGATGACTATA  
CATATAAATGATTACCATATTATGGTCAGAAATTGTATAACAGTGTTAGAATATTCTGTG  
AAGACTTTTTTAACACAATATTCTGTGAAGACTAGATATCATGTACTTCTCCTTGTTTTCT  
TTGACCTGATGTCCTTCGTCACATGTTGTGCTCCTCACAAAAAATAGCAAGCACATGTT  
TCAAATAATTGTTAATAATATAATTAGCCTTTAATTTATATGGTTCTATTTTGAGATAT  
TTTTGTAGTCCAACCTTATATATTTGTGACTATTCTCAAAAACAAAACCTTATATATGTGTG  
CCTCTCAAATGTAGGGAGTGTCTTGGAATGGCAAACGGGTCCGCATTACTTTTGCTTG  
TGTTCCATCTTCTCTTCAAGATGGTCTCGGAAGGATCAAATCATTCTGTCAAAGGAACAA  
GAAGAGAAATTCGAGCGATGATTGCTAGTTGTATATCTGACTGAAGCTGTAAATCATTCC  
CAGTATCCCCATCTATATCTTTCAATAAAATGGAACCTTTTAGTTCTCTATGAATAGAAGT  
CAACATCTCCTTGAATATGTTCTGGTTGTTGTGGCCTGGACGAAACATAGTGAATGTTAT  
GTTAGTGAAGTTACATTGGCGTCGAAGATCTTTGAAGTTTTTTTTTTTTTTGGGGGGGG  
GGGGGGGGGGTGCTTTGATATTACTCTTAAGTACACGTTCTCTCAAGTTATGTCAAAGCA  
CTTTGTAAACAATTGTAGATTTGGTATCATGATATGGATTAAACTAGTCAGATACTTGGT  
AAGCACAAACCCTACCTATGTTAGGCTCACTAAGGTGGCGTTTGGTTTCGAGAGAGAGGAA  
GGATCAGTTGATGATATCCCCAATCATCGAAGTAAATCATGTGTTGTTGCTACCACTTTT  
CTACAATCCTAGTAGCTGCATGCGTTGAGCTACTGATCAACACCACTGCACAACCATATT  
CTCTGTGCAAAATCGGCACCCAAAGATTACATCTCACAGCTGAAGCAACCACCAATTTG  
AAGAGAGGAACCCTCACAAAGACCTTTGAGTGCCCCCACAATGCATGGTTAGGCCGCCG  
TCGCAGGCCGGAGTGGTCACCATGCGGACCAACACCAACTCCAACGGGGGAGCACGTCAC  
CGATTACTGAAATTCCCCAAACAATTCTTAATTTGTGAACAAAATTTAAAAACAGGAACA  
ATTTTTGAATTTGTGAACAAATTTTTTAAACGGGTATTCTCTGAACATTTTTTCAAAATTGT  
GATCAAAATTTTAAAAACGACTTCTTTCTCAAATTTGAGCAATATTTAAAAATTATAAAAA  
GTTCAACAATTTTGAACTTTTTAAAAATTAGCGAGAACATTTTGAAATTTCTAAATATTTT  
CGAATTTGGAACATTTTTTCTATTTCTGAACAAAATTTGAAAATACGAACGTAATTTGGA  
ATAAATTTTGGAATAATGCGATTTTTTGAATTTCTGAACATATTTTGAAAAACAAAAAA  
CTTTAAAGGTAAAAATAAAATAAAATAAAATAGAAACATAAAAAATAAGCAAAAAATA  
AAAGAAATCCGAGAAAAGCCAACTGGGAATAGCACATGGAAAAACCCAGCCGTCCGCCGC  
ACTGTGTAAAGCTATAAGTGAGCCGCCCAAGCCTCGTCTCATCATACCCTGTGCGA  
AACCCCGACAATTCGTTGCACATATGCGGCGAATAGGCTTTTCCAGGAGCTCCTGTCTTCC  
GGTTATGGGTCAATTTGCACACCCCTCCTCCACTTGGGCCAGGCTATTATACTTTTTTTCC  
TTCTTTTCGACCTCACGTTACTACGCCAGTTTAGTTTTTTGGAAGCGACCAACCGGTTTTGT  
GAAGGTTCTAGAACTCAACCATTTTTTGGGAAGCTTCTAGAAGCCTATGAATGTTTCTTT  
TGGACATGTATTATTGTGTTTTTTCTTTTTTCAAATTGCACAATCTTTTTTCAAATTCAT  
GATTTTTGTGAACTTGTGATTTTTTGAATCCGTGATTTTTTTTTCTAAATCCGTGTTTT  
GAAAAAACTGTGGACTTTTCCGAAATTAATGAACATTTGTTTGCAAGATCGATGATCCT  
TTTCAAATGAGCGATTTTTTTCTAAATATCCACATATTTTTCATATTCATAAGCTTTCC  
TTTTAATCGTGAACATCTTAGCATTTGGTGAACTTTTATTAATTTTCTTTATAAAATGA  
TTTTTTTTTCAAAGCCAACGGTTAACGGTTGACCGCTGAACCACAACCACAAACGGGGA  
AACCATTGACTCGCTGAACAGGGCAGGGCTTTCATATGATTGGGTGGTCTAATACCAGCG  
CCCCTGACTACTAAACGAAGGAATTGCAAATTTTACCAACCCTACTATGGTAAAAATG  
AATATCACGATAAAAAAGGGGAAAAAAACTATACCCTGAAAATCCCTCTGTTTTCTAAAT  
ATTTGTTGTTGGGGGAGTAATACTGAAAGAACTAATCTAGTTCTCCGCAATAACAAATA  
TTATGATTCGGGGGAGTATAACTATTACACGATCAACCAAAGAATGTCCTCCAAGAAAA  
ACCCAAAGAAAGTGCTAGAGTTTTGTTTTCAAGGACCGAAAGATAGAGATAGCATTCTGA  
ATTAGGTCCATCTTTTTTCCAAGGATTGAAAGAAAGAGATAGAATTCTGAATTAGGTGCG

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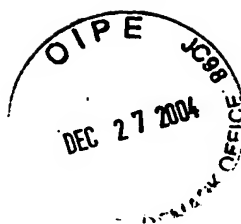
FIG. 9C

GAGATATCATTTCTGGATTAGGTACAATTGTTTTGCCGGCACAGCCAAACCCCGCAGTGG  
AGCCGGAATTGGAATTGAGTGGGTGGAGTCGAGAAGCATGGTTCATGCGTTCTCAAAGAG  
TGTAGCCAGTAGTGTGTGCTCCTTGGTGCTGGAGCTGCATATACAAGTACATAAAACAAA  
GACGATCAGCTGGCAGCGTGCCTGCATGCGTGCTTCTTGCTGCCGCCCCGGAAGCCCCGG  
TTGATGTGCGCAGGCGAGTGGCGACGGGACCGACGGCTATAAAGCACGGCCAAGCACCGC  
CGCCGTTCTCAATCCATCCATCCCTTAGCTGATTTGATTGACTAGCTAGTTTCATTCCCTG  
CCACACTGCTAGTACTCCTCCTCGTTTCCCTCGTGGCAATGGTACACCAGAGCAACGGCCA  
CGGCGAGGCCGCCGCCGCCGCCGCCAACGGCAAGAGCAACGGGCACGCCGCCGCCGCCGAA  
CGGCAAGAGCAACGGGCACGCGGCGGGCGGGCGGGTGGAGTGGAAATTTGCCCGGGGGCAA  
GGACGGCATCCTGGCGACGACGGGGGCGAAGAACAGCATCCGGGCGATACGGTACAAGAT  
CAGCGCGAGCGTGGAGGAGAGCGGGCCGCGGCCCGTGCTGCCGCTGGCCCACGGTGACCC  
GTCCGTGTTCCCGGCCCTTCCGCACGGCCGTCGAGGCCGAGGACGCCGTCGCCGCCGCCGCT  
GCGCACCGGCCAGTTCAACTGCTACGCCGCCGCCGCTCGGCCCTCCCCGCCGCACGAAGGTA  
ACATTTACAGCTTACCCGTAATGTATGCGTGAGCATGCATGCGCCGGTTTACTTACGTGC  
CCGCCGCTGTTCTTCCCCGGTGCGTTCAAATTTTAACCTTCTATAAGTACCTTATAAAA  
ACAAACAGCGCCGTAGCAGAGCACTTGTACAGGGCGTGCCCTACAAGCTATCGGCCGAC  
GACGCTTCCCTACCGCCCGCGGAACCTCAGGCGATCGAAGTCATAATCCCGGTGCTGGCC  
CAGACTGCCGGCGCCAACATACTGCTTCCCCGCCGAGGCTATCCAAATTACGAGGCGCGA  
GCGGCATTCAACAAGCTGGAGGTCCGGCACTTCGACCTCATCCCCGACAAGGGGTGGGAG  
ATCGACATCGACTCGCTGGAATCCATCGCCGACAAGAACCACCGCGATGGTCATCATA  
AACCCAAACAATCCGTGCGGCAGCGTTTACTCCTACGACCATCTGGCCAAGGTTTTCAT  
CCATGCATCCTCTGCCTCGTTGATCGACCGGTCTGTTTGAACATAGTATATGGATTGCGT  
TTGCTAATCGTGTGCTGATGATGCTGTTTGGTTATCAGGTGCGGGAGGTGGCAAGGAAGC  
TCGGAATATTGGTGATCGCTGACGAGGTTTACGGCAAACCTGGTTCTGGGCAGCGCCCCGT  
TTATCCCGATGGGCGTCTTTGGGCACATTGCCCGGGTCTTGTCATTGGATCTCTGTCCA  
AGTCGTGGATAGTGCCCTGGATGGCGACTTGGATGGGTGGCGGTGTACGACCCACAAAGA  
TTTTAGAGAAAAC TAAGGTAGCTTTAGCTCCCTATCATTCCTCTCATATGCTACTGTGGG  
GATTAGTATTTTGTCTAAATTTGTACTGCCTTTGTTTATTCAGATCTCTACGTCTATTAC  
GAATTACCTTAATGTCTCAACGGACCCAGCAACCTTCGTTTACGGTTAGTCTTTGGTTCTT  
GCCCTATTTTGTCTCATGTCCCTGTGTTGCATGTCAAATGACCGGCTTCAAGTTAGTATAT  
AGAGTTTTTGTAAAGTGTGAATGTGCAAGTCCAACATGATGGAAGAAAGATACATCTATT  
TTTAGTCATTCCCTTTGTTTGTGTTGATTCCATAAAATAAATAAACACAAAGCCAGAACC  
AACTATTGAATAGAATAATTTTCTTAGAAAATATACATTGTATTTTGGAGCATGCCATAT  
TCTTTTCGATCAAGTATGCAATATATTAACCTTGCATTGTACTACGAGTATACCATGTT  
GTTAAGAATTTCTTTACCTACAACACCTTGTCTCGCATCTTCATATTTTGATATCCTTGA  
CATTATTGTTCTCTTATGATTACACAACCTTAATTATGGATTTTTTGTGCTATCAAATTGT  
TTAGGAAGCTCTTCTTAAATTTCTTGAGAACACAAAAGCAGATTTCTTTAAGAGGATTAT  
TGGTCTACTAAAGGAATCATCAGAGATATGTTATAGGGAAATAAAGGAAAACAAATATAT  
TACGTGTCCCTCACAAGCCAGAAGGATCGATGTTTGTAAATGGTAAGCTAAGCATAGACTTA  
CTTTTAAAGGTTAATCTGGGATCTCAGTGCATCCAACAAACAATCAAATCAAATATAAT  
TATGTTTTGTCTATGGATCTTTTTGAAGATGCATGCATTTGAAGAATAATGAAGAGAGTTG  
AAATTATTTTAGGACTAATCTTCCGTATATCATTTGTCCATTTTTTTGTTATTACTGTAA  
ATTGGTAACACTCAAATCATATTACAAAAGTTTCCCTCCCATTTTTTAGTAAGATTGACTT  
CCTTTCTATAACCATGTATTAACTTCCATGTAAACAGGTCAAACCTAACTTACATCTTTT  
GGAGGAGATCCATGACGACATAAATTTTTGCTGCAAGCTCGCAAAGGAAGAATCTGTAAT  
TTTATGTCCAGGTAGGAATGTATATGGCCATTTTAAAGGAAAACCTATATGGAATAATAAT  
ATCTTCTTGTATATACTAAACAATACTTCCCTCCATCCTAAAATAAATGTCTTACACTTAGC  
ACAATTTTATACTAGATCTAGTACAAAGTTGAAACAGTTATTTTGGGACAGAGGGAGTAG  
TATATATTGTGTGAGAACATAAGGTTATGTTTACTGATATATGCTTCTTAAATGTGAAA  
CATGTTCTCTTATGTTTTTTGATTGTATACGAAGTTCTTATCAGTTTCCGAGATGACTAC  
ACATAAATGATTACCATATCATTTGTGCAAAATGTATTACCACATTAGAATATCTTTCT  
TTTTATGCAAAGACTAGCATGGCATGTACTTTTCCCTGTACCTATGTGTCTTTTTTTTTTC



# FIG. 9D

TCGTTACATGTTTGTGCTTCTCACAAAAATAATAATACCAAGCACATGTTCCAAATGATT  
ATTAATAATTTTGAGGTGTTTTTCAACCAACTTATATACTTTCATAGTTCTAAAAAACC  
GTATATATGGTTAACTCTAACAAAAACTTATATATGTTTTCTCTCTAATACAGGGAGTGT  
TCTTGGAATGGAAAATTGGGTCCGTATTACTTTTTGCCTGCGTTCCATCTTCTCTTCAAGA  
TGGACTCGAAAGGGTCAAATCATTCTGTCAAAGGAACAAGAAGAAGAATTCTATAAATGG  
TTGTTAGTTGTACACACCCCTAGTTGTACATCTGACTGAAGCTGTAAATCATTCTAGTT  
ATCCCCATTATATATTTCAATAAAACATATTGTAATGGTCTGTGTAGCTGTCCAAGT  
CATGTACTCTACTTTTTTGATGTATTTGGCCTCATTGCCTTGCATCAGTTTCAATAAAAAT  
GGTGTGTACACAATGATGATGTAGAGGCGAGGTGTTTTGACCACCTTTTCAACAAAAAT  
CTATATCTTTCAACAAATGAAACCTTGAGTTCCCTTTGAGTAGAAGTCAACATACTCCTT  
GAATATGCTATGGTTTCCATGGTCTGGATGAAACATGATGAATAGAAGTGAAGTTATATC  
CATGTCAAAGTTTTTTAATGTTTAATTTTATTATGAGAACTTTGATATTACTTCTAGCAC  
ACATTCTCTGAAGTAATTGTCAGTTTGGTACTTGAAGGGACCTATATTTTTCTATTGGG  
GGGGGGGGTGAATAGGCGGTTTATAACCAATTGTATATTTGAGAATATCTTAATGTGGA  
ATTAACTAGGTGAATATTTTTTCCAATAAAGGTGCTTTTATTGACTCACAATGTACCA  
TCAAGGGATACAATCATAATGAGTACACAATCGACATCTACATAATCAGGTTGCATACGG  
CCAACACACACACACGCACACACACATTACACACACAAAATCATGCTGACGAAGAGCGAA  
GTCATACAAGATCAAACTATGCCTAGGCGGAGGAAGAATAGAAAAACATGAAGAAATGA  
AAAACCGTGACTGACAACATACTGACCATCGACGACAAACATCTGTAGACAACACAAAAA  
CTGCGAGAAAAGTTCTATAAACTGGCGCCTTCGAGAAGGAAACGACGTGCAAGAGTTGC  
CATCATCGGATCCAACCACTAAGGTCATATCCTGGGTTTTTCATCCTGAAGATCAAAATCCG  
AGCAAACTCCGAGTAATGTCTTTATTAGGGTAACGATTCAAAAAATGCCACAATCATGAG  
TTATGACCAATTAGACCAGACCTAGGATTTTTATCCAAAGCTCGAGACGGGTACTCTAGA  
AGTACCATCCAATTGAAGTCATCCCACTTGCCCTCAATACAAATAGTTGCATAGATGCACG  
GTCCATATGGCGAGTAATGGACATGAGCGCGCATGTGTAGGTTAACGTGACGTGACAAGA  
GCCTGTGCGCCACCACTCGACGAAGTGTTTGTATGGGGAGGAAGAAGTATGGCTCCACCAAC  
ATCCCAAGTTTGAAACATTCTAGAGCCCTTACCATACTCACAAAGCGACAATTGATGAC  
TATCTGTATCAGACGACAAATCCATGTCCGTCCTCGCTCTATCTTGGTCATTGACATAC  
TACCTGGCAAAGGCGGATTCAAGCCCCAGACAGCCTGGGCGGCCGC



# FIG. 10 A

ctcgatcccattgcaatggtatgattagctatcaaacgaaagaaagagatggcatgtgcc  
ctgtgtgtcatccctcactggcttggcgaatggcgataccgagttaggtagagtgttttt  
ttagcatgatgtctgcccgcactgccaaagaaaactgcgtgcagcggactgcaggagagt  
gagcatgcatgctttgtgatgagcggagctgagtggtgtcactaactgaacccaatca  
gcattgggtgagtcgagtcgagaagcatcatgcttccctgcgtcccgatccgcttatcttt  
ttctcccaaattattaaagagggatagatgatggtgtgctgggttgggttagagtacgtgc  
atagaaccaaagcgaggcgccgaaaatatgccggggataatggtggcaggccgcaacggc  
cacgcccgtcagctggcagcggcgtgccagagcgtgccagagcgtgcgcgcgtgcgtgct  
tcttgcgtgccggccccggttcgtgtgcggtcagagcaacggctatataggaccgtcaatc  
accgctactcaatccgtccccaactcggttctctattacCGCTACTAGTAGTATTCTCTGGT 600

GTAGTCTAGTAGTACTCCTCCTCCTTCTCCTCCTACCCGTTTCCTCATGGCCACCGT  
M A T V NAAT-B

ACGCCAGAGCGACGGAGTCGCCGCGAACGGCCTTGCCGTGGCCGCAGCCGCGAACGGCAA  
R Q S D G V A A N G L A V A A A A N G K

GAGCAACGGCCATGGCGTGGCTGCCGCGTGAACGGCAAGAGCAACGGCCATGGCGTGGA  
S N G H G V A A A V N G K S N G H G V D

TGCCGACGCGAACGGCAAGAGCAACGGCCATGGCGTGGCTGCCGACGCGAACGGCAAGAG  
A D A N G K S N G H G V A A D A N G K S

CAACGGCCATGCCGAGGCCACTGCGAACGGCCACGGCGAGGCCACTGCGAACGGCAAGAG  
N G H A E A T A N G H G E A T A N G K T

CAACGGCCACCGCGAGAGCAACGGCCATGCTGAGGCCGCGACGCGAACGGCGAGAGCAA  
N G H R E S N G H A E A A D A N G E S N

CGAGCATGCCGAGGACTCCGCGGCGAACGGCGAGAGCAACGGGCATGCCGCGGCGGCGGC  
E H A E D S A A N G E S N G H A A A A A

AGAGGAGGAGGAGGCGGTGGAGTGGAATTTCCGCGGTGCCAAGGACGGCGTGCTGGCGGC  
E E E E A V E W N F A G A K D G V L A A

GACGGGGGCGAACATGAGCATCCGGGCGATACGGTACAAGATCAGCGCGAGCGTGACAGGA  
T G A N M S I R A I R Y K I S A S V Q E

GAAGGGGCGCGGCCCGTGCTGCCGCTGGCCCACGGGGACCCGTCCGTGTTCCCGGCCTT 1200  
K G P R P V L P L A H G D P S V F P A F

CCGCACGGCCGTGAGGCCGAGGACGCCGTGCCGCGCGCTGCGCACCGGCCAGTTCAA  
R T A V E A E D A V A A A L R T G Q F N

CTGCTACCCCGCCGGCGTCGGCCTCCCCGCCGCACGAAGgtaacaacaacaacaacacaa  
C Y P A G V G L P A A R S

gaacaatttcttttgcgtgtcgtgtcgcgcggcaatccatgcatgcgcatgtgccgct  
ttcacgtgtccgtccgtccgtccacggttcttctctctccctacgcccatgagaaatct

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FIG. 10 B

A V A E H L

S Q G V P Y M L S A D D V F L T A G G T

Q A I E V I I P V L A Q T A G A N I L L

P R P G Y P N Y E A R A A F N R L E V R

H F D L I P D K G W E I D I D S L E S I

A D K N T T A M V I I N P N N P C G S V

Y S Y D H L S K

V A E V A K R L G I L V I A D E V Y G K

L V L G S A P F I P M G V F G H I T P V

L S I G S L S K S W I V P G W R L G W V

A V Y D P R K I L Q E T K

I S T S I T N Y L N V S

T D P A T F I Q

2400

A A L P Q I L E N T K E D F F K A I I G

CTGCTAAAGGAATCATCAGAGATATGCTACAAACAAATAAAGGAAAACAAATACATTACA  
L L K E S S E I C Y K Q I K E N K Y I T

TGTCCTCACAAGCCAGAAGGATCAATGTTTGTTCATGgtaagcctatthttgtgaagtaaaa  
 C P H K P E G S M F V M

aaatcttagggagtgtagtaatcataaacttatttatataggattaatctgggaccgaa 3000  
atgcatccaacataattacttcaaattcaaattcaaattacattcttccgtacatatattt  
tgaagatgcatgtattttaagaataatgacgagagctaaagttatgctacgactaatcat  
ctggatatcctttgtccatcttttgttatactgtggaatgttaatggtaaatacatatt  
acacaaatatccatgctagtttctagaaagattgattatctgttaaccatgaactcc  
gtattaacttccatgtaaacagGTGAACTGAACCTTACATCTTTTGGAGGAAATAGACGA  
V K L N L H L L E E I D D

TGACATTGATTTTGTCTGCAAGCTCGCAAAGAAGAATCAGTAATCTTATGCCCAGgtag  
D I D F C C K L A K E E S V I L C P

gaatccattgttgatttttgactgtatatgaagttcttatcaatttccgagatgactata  
catataaatgattaccatattatggtcagaaattgtataacagtggttagaataattctgtg  
aagacttttttaacacaatattctgtgaagactagatatcatgtacttctccttggtttc  
ttgacctgatgtccttcgtcacatgtttgtgctcctcacaaaaaaatagcaagcacatggtt 3600  
tcaaataattgttaataatataaatttagcctttaaatttatatggttctattttgagatat  
ttttgtagtccaacttatataattttgtgactattctcaaaaacaaaacttatatatgtgtg  
cctctcaaatgtagGGAGTGTTCTTGGAATGGCAAACCTGGGTCCGCATTACTTTTGCTTG  
G S V L G M A N W V R I T F A C

TGTTCCATCTTCTCTTCAAGATGGTCTCGGAAGGATCAAATCATTCTGTCAAAGGAACAA  
 V P S S L Q D G L G R I K S F C Q R N K

GAAGAGAAATTTCGAGCGATGATTGCTAGTTGTATATCTGACTGAAGCTGTAAATCATTC  
K R N S S D D C \*  
CAGTATCCCCATCTATATCTTTCAATAAAATGGAACCTTTAGTTCTCTATGAATAGAAGT

CAACATCTCCTTGAATATGTTCTGGTTGTTGTGGCCTGGACGAAACATAGTGAATGTTAT

GTTAGTGAAGTTAcattggcgtcgaagatctttgaagttttttttttttttttttgggggggg

ggggggggggtgctttgatattactcttaagtaacacggttctctcaagttatgtcaaagca  
ctttgtaaaccaattgtagatttgggtatcatgatatggattaaactagtcagatacttgggt 4200  
aagcacaacccctacctaattgtaggctcactaagggtggcgtttgggttcgagagagaggaa  
ggatcagttgatgatatccccaatcatcgaagtaaattcatgtgttgttgctaccactttt  
ctacaatcctagtagctgcattgagctactgatcaacaccactgcacaacccatatt  
ctctgtgcaaaatcggcaccacaagattacatctcacagctgaagcaaccaccaaatttg  
aagagaggaaacccctacacaagacctttgagtgccccccacaatgcatggttaggcgcgcg  
tcgcaggccggagtggtcaccatgcggaccaacaccaactccaacgggggagcacgctcac  
cgattactgaaattccccaacaattcttaatttgtgaacaaaatttaaaaacaggaaca  
atttttgaatttgtgaacaaatttttttaaacgggtatttcctgaacatttttcaaaattgt  
gatcaaaatttttaaaacgacttctttctcaaatgtgagcaatattttaaattataaaaaa  
gttcaacaattttgaacttttttaaaaatttagcgagaacattttgaaattctaaatatttt 4800  
cgaatttggaacattttttctattttctgaacaaaaattgaaaatacgaaacgtaatttgga  
ataaatttttgaaaatgcgattttttgaaattttctgaacataattttgaaaaacaaaaaa  
ctttaaaagggtaaaaataaaaataaaaataaaaatagaaacataaaaataagcaaaaaata



FIG. 10 D

aaagaaatccgagaaaagccaactgggaatagcacatggaaaaaccagccgtccgcgc  
actgtgtaaagctataagttagccggcccaagcctcgtcgtctcatcataccctgtgoga  
aaccgccgacaattcgttgcaactatgoggcgaataggcttttccaggagctcctgtcttcc  
ggttatgggtcatttgcacacccctcctccacttgggccaggctattatacttttttcc  
ttcttgcacctcacgttaactacgccagtttagtttttgggaagcgaccaaccggttttgt  
gaaggttctagaaactcaaccatttttgggaagcttctagaagcctatgaatgtttcttt  
tggacatgtattatttgtgttttttcttttcaaattgcacaatcttttttcaaattcat 5400  
gatttttgtgaaacttgtgattttttgaatccgtgatttttttctaaatccgtgtttt  
gaaaaaaactgtggacttttccgaaattaatgaacatttgtttgcaagatcgatgatcct  
tttcaaattgagcgatttttttctaaaatatccacatatttttcatattcataagctttcc  
ttttaatcgtgaactatcttagcatttgggtgaacttttattaattttctttataaaatga  
ttttttttcaaagccaacggttaacggttgaccgctgaaccacaaccacaaaccgggga  
aaccattgactcgtgaacagggcagggctttcatatgattgggtggtctaataccagcg  
cccctgactactaaacgaaggaattgcaaattttaccaaccactactatggtaaaaaatg  
aatatcacgataaaaaaggggaaaaaaaactataaccctgaaaatccctctgtttctaaat  
atttgttgttggggagaactaatctgaaagaactaatctagtctccgcaataacaaata  
ttatgattcggggggaggtataactattacacgatcaaccaaagaatgtcctccaagaaaa 6000  
accaaagaaagtgcctagagttttgttttcaaggaccgaaagatagagatagcattctga  
attaggtccatcttttcccaaggattgaaagaaagagatagaattctgaattaggtgcg  
gagatatcatttctggattaggtacaattgttttgcgggcacagccaaaccccgcagtgg  
agccggaattggaattgagtggtggagtcgagaagcatggttcatgcgttctcaaagag  
tgtagccagtagtggtgctccttgggtgctggagctgcataatacaagtaataaaacaaa  
gacgatcagctggcagcgtgcctgcagtcgtgcttcttgcgtgcgcgcccggaagcccgg  
ttgatgtgcgcagggcagtgggcgacgggaccgacggctataaagcacggccaagcacccg  
cgccgttctcaatccatccatcccttagctgatttgATTGACTAGCTAGTTTCATTCCTG

CCACACTGCTAGTACTCCTCCTCGTTTCCTCGTGGCAATGGTACACCAGAGCAACGGCCA  
M V H Q S N G H NAAT-A

CGGCGAGGCCGCCGCCGCCGCCGCAACGGCAAGAGCAACGGGCACGCCGCCGCCGCGAA 6600  
G E A A A A A N G K S N G H A A A A N

CGGCAAGAGCAACGGGCACGCCGCCGCCGCCGGTGGAGTGGAATTTGCCCCGGGGCAA  
G K S N G H A A A A A V E W N F A R G K

GGACGGCATCCTGGCGACGACGGGGGCGAAGAACAGCATCCGGGCGATACGGTACAAGAT  
D G I L A T T G A K N S I R A I R Y K I

CAGCGCGAGCGTGGAGGAGAGCGGGCCGCCGCCCGTGCTGCCGCTGGCCACGGTGACCC  
S A S V E E S G P R P V L P L A H G D P

GTCCGTGTTCCCGGCCTTCCGCACGGCCGTCGAGGCCGAGGACGCCGTCGCCGCCGCGCT  
S V F P A F R T A V E A E D A V A A A L

GCGCACC GGCCAGTTCAACTGCTACGCCGCCGNNTCGGCCTCCCCGCCGCACGAAGgta  
R T G Q F N C Y A A G V G L P A A R S

acatttacagcttcaccgtaaatgtatgcgtgagcatgcatgcgcgggtttacttacgtgc  
ccgcgcgtgtttcttcccgggtgcgttcaaaatttttaaccttctataagtaaccttataaaa  
acaaacagCGCCGTAGCAGAGCACTTGTCACAGGGCGTGCCCTACAAGCTATCGGCCGAC  
A V A E H L S Q G V P Y K L S A D





FIG. 10 E

GACGTCTTCTCACC GCCGCGGAACTCAGGCGATCGAAGTCATAATCCCGGTGCTGGCC  
D V F L T A G G T Q A I E V I I P V L A

CAGACTGCCGGCGCCAACATACTGCTTCCCCGGCCAGGCTATCCAAATTACGAGGCGCGA 7200  
Q T A G A N I L L P R P G Y P N Y E A R

GCGGCATTCAACAAGCTGGAGGTCCGGCACTTCGACCTCATCCCCGACAAGGGGTGGGAG  
A A F N K L E V R H F D L I P D K G W E

ATCGACATCGACTCGCTGGAATCCATCGCCGACAAGAACACCACCGCGATGGTCATCATA  
I D I D S L E S I A D K N T T A M V I I

AACCCAAACAATCCGTGCGGCAGCGTTTACTCCTACGACCATCTGGCCAAGgttttgc  
N P N N P C G S V Y S Y D H L A K

ccatgcacccctctgcctcggtgatcgaccggtctgtttgaacatagtatatggattgcgt  
ttgctaatcggtgtgctgatgatgctgtttggttatcagGTCGCGGAGGTGGCAAGGAAGC  
V A E V A R K

TCGGAATATTGGTGATCGCTGACGAGGTTTACGGCAAACCTGGTTCTGGGCAGCGCCCCGT  
L G I L V I A D E V Y G K L V L G S A P

TTATCCCGATGGGCGTCTTTGGGCACATTGCCCGGTCTTGTCCATTGGATCTCTGTCCA  
F I P M G V F G H I A P V L S I G S L S

AGTCGTGGATAGTGCCTGGATGGCGACTTGGATGGGTGGCGGTGTACGACCCCAAAAGA  
K S W I V P G W R L G W V A V Y D P T K

TTTAGAGAAACTAAGgtagcttttagctccctatcattcttctcatatgctactgtggg  
I L E K T K

gattagtatTTTTgctaaatttgtactgcctttgtttattcagATCTCTACGTCTATTAC 7800  
I S T S I T

GAATTACCTTAATGTCTCAACGGACCCAGCAACCTTCGTTCAAGgtagtctttggttctt  
N Y L N V S T D P A T F V Q  
gccctattttgtcatgtccctgtgttgcatgtcaaatagaccggcttcaagtagtatat  
agagtttttgtaagtgtgaatgtcgaagtccaacatgatggaagaaagatacatctatt  
tttagtcattccccctttgtttgtttgattccataaaataaaataaacacaaagccagaacc  
aactattgaatagaactatttttcttagaaaataacattgtattttgagcatgccatat  
tcttttcgatcaagtatgcaatatattaaaacttgcatgtactacgagtataccatgtt  
gttaagaattttctttacctacaacaccttgctcgcacatcttcataattttgatataccttga  
cattattgttctcttatgattcacacaacttaattatggattttttgtgctatcaaattgt  
ttagGAAGCTCTTCTAAATTCCTTGAGAACACAAAAGCAGATTTCTTTAAGAGGATTAT  
E A L P K I L E N T K A D F F K R I I

TGGTCTACTAAAGGAATCATCAGAGATATGTTATAGGGAAATAAAGGAAAACAAATATAT 8400  
G L L K E S S E I C Y R E I K E N K Y I

TACGTGTCCTCACAAGCCAGAAGGATCGATGTTTGTAATGgtaagctaagcatagactta  
T C P H K P E G S M F V M



FIG. 10 F

ctttttaagggttaatctggtatctcagtgcatccaacaacaatcaaatacaaatataat  
tatgttttgctatggatctttttgaagatgcatgcatgttgagaataatgaagagagttg  
aaattatttttaggactaatcttcctgatatcatttgtccatttttttgttattactgtaa  
attggtaacactcaaatacattacaaaaagtttctcccattttttagtaagattgactt  
cctttctataaccatgtatttaacttccatgtaaacagGTCAAATAAACTTACATCTTTT  
V K L N L H L L

GGAGGAGATCCATGACGACATAAATTTTTGCTGCAAGCTCGCAAAGGAAGAATCTGTAAT  
E E I H D D I N F C C K L A K E E S V I

TTTATGTCCAGgtaggaatgtatatggccatttttaaaggaaaactatatggaataataat  
L C P

atcttcttgtttataactaaacaataacttctccatcctaaaataaatgtcttacacttagc  
acaattttatactagatctagtacaaagttgaaaaggttattttgggacagagggagtag 9000  
tatatatgtgtgagaacataagggttatgtttgactgatatatgtcttctaaatgtgaaa  
catgttctcttatgttttttgattgtatacgaagttcttatcagtttccgagatgactac  
acataaatgattaccatatcattgtcgaaaaatgtattaccacattagaatattctttct  
ttttatgcaaagactagcatggcatgtacttttcttgtacctatgtgtcttttttttttc  
tcgttacatgtttgtgcttctcacaaaaataataaccaagcacatgttccaaatgatt  
attaataattttgaggtgtttttcaaccaacttatatactttcatagttctaaaaaaacc  
gtatatatggttaactctaacaaaaacttatatatgttttctctctaataacagGGAGTGT  
G S V

TCTTGGAATGGAAAATTGGGTCCGTATTACTTTTGCCTGCGTTCCATCTTCTCTTCAAGA  
L G M E N W V R I T F A C V P S S L Q D

TGGAATCGAAAAGGTCAAATCATTCTGTCAAAGGAACAAGAAGAAGAATTCTATAAATGG  
G L E R V K S F C Q R N K K K N S I N G

TTGTTAGTTGTACACACCCCTAGTTGTACATCTGACTGAAGCTGTAAATCATTTCTAGTT 9600  
C \*

ATCCCCATTTATATATTTCAATAAAACATATTGTAATGGTCTGTGTAGCTGTCCAAGT

CATGTAATCTACTTTTTGATGTATTTGGCCTCATTGCCTTGCATCAGTTTCAATAAAAAAT

GGTGTGTACACaatgatgatgtagaggcgaggtgttttgaccaccttttcaacaaaaat

ctatatctttcaacaaatgaaaccttgagttccctttgagtagaagtcaacataactcctt  
gaatatgctatggtttccatggtctggatgaaacatgatgaatagaagtgaagttatatac  
catgtcaaagtttttttaattgtttaatttcattatgagaactttgatattacttctagcac  
acattctctgaagtaattgtcagtttggtacttgaagggaacctatatttttccatttggtg  
gggggggggtgaataggcggtttataaccaattgtatatttgagaatatcttaattgtgga  
attaaactaggtgaatattttttccaataaagggtgctttttattgactcacaaatgtacca  
tcaagggatacaatcataatgagtacacaatcgacatctacataatcaggttgcatacgg 10200  
ccaacacacacacacgcacacacacattcacacacacaaatcatgctgacgaagagcgaa  
gtcatacaagatcaaaactatgcctaggcgaggagaagaatagaaaaacatgaagaaatga  
aaaaccgtgactgacaacatactgaccatcgacgacaaacatctgtagacaacacaaaaa  
ctgcgagaaaaagttctataaaaactggcgcttctcgagaaggaaaacgacgtgcaagagttgc  
catcatcggtatccaaccaactaagggtcatatcctgggttttcatcctgaagatcaaatccg  
agcaaaactccgagtaattgtctttattagggttaacgattcaaaaaatgccacaatcatgag



FIG. 10G

ttatgaccaattagaccagacctaggatttttatccaaagctcgagacgggtactctaga  
agtaccatccaattgaagtcatcccacttgctcaatacaaatagttgcatagatgcacg  
gtccatatggcgagtaatggacatgagcgcgcgcatgtgtagggttaacgtgacgtgacaaga  
gcctgtcgccaccactcgacgaagtgtttgatggggaggaagaagtatggctccaccaac 10800  
atcccaagtttgaaacattotagagccccttaccatactcaciaagcgacaattgatgac  
tatctgtatcagacgacaaatccatgtccgtcactcgctctatcttggtcattgacatac  
tacctggcaaaggcggattcaagccccagacagcctgggcggccgc

Application No.: 10/019,783

Docket No.: SAE-0005



**REPLACEMENT SHEETS**